CLAIMS

What we claim is:

1. A composition for delivering a therapeutic agent across the oral mucosa comprising:

   at least one therapeutic agent at least partly in an ionized form, the ionized form capable of being converted into an un-ionized form;

   a carrier; and

   a buffer system,

   wherein the buffer system comprises at least two different buffering agents and is capable of changing the pH of saliva from an arbitrary initial pH to a predetermined final pH, independent of the arbitrary initial pH, and of sustaining the predetermined final pH for a period of time, and

   wherein the buffer system favors substantially complete conversion of the ionized form to the un-ionized form.

2. The composition of claim 1 wherein the at least one therapeutic agent is basic.

3. The composition of claim 2 wherein the at least one therapeutic agent is selected from the group consisting of alfentanil, allylprodine, alphaprodine, anileridine, benzylmorphine, bezitramide, clonitazene, codeine, dextromoramide, diampromide, dihydrocodeine, dimenoxadol, dimepheptanol, dimethylthiambutene, dioxaphetyl butyrate, dipipanone, ethoheptazine, ethylmethylthiambutene, ethylmorphine, etonitazene, fentanyl, heroin, hydrocodone, isomethadone, levophenacylmorphan, lofentanil, meperidine, methadone, morphine, narceine, nicomorphine, norlevorphanol, normethadone, norpipanone, opium, oxycodone, papaveretum, phenadoxone, phenoperidine, piminodine, piritramide, propheptazine, promedol, properidine, propiram, propoxyphene, sufentanil, tramadol, tilidine, analogs, and mixtures thereof.

4. The composition of claim 3 wherein the at least one therapeutic agent is oxycodone.

5. The composition of claim 1 wherein the at least one therapeutic agent is acidic.

6. The composition of claim 5 wherein the at least one therapeutic agent is montelukast.

7. The composition of claim 1 wherein the at least one therapeutic agent is amphoteric.

8. The composition of claim 7 wherein the at least one therapeutic agent is selected from the group consisting of buprenorphine, butorphanol, cyclazocine, desomorphine, dezocine, dihydromorphine, eptazocine, hydromorphone, hydroxypethidine, ketobemidone, levallorphan, levorphanol, meptazinol, metazocine, metopon, morphine, nalbuphine, nalorphine, naloxone, naltrexone, normorphine, oxymorphone, pentazocine, phenomorphan, phenazocine, analogs, and mixtures thereof.

9. The composition of claim 2 wherein the predetermined final pH is within a range of from about 7.1 to about 11.5.

10. The composition of claim 2 wherein the predetermined final pH is within a range of from about 9 to about 11.

11. The composition of claim 5 wherein the predetermined final pH is within a range of from about 2 to about 6.9.

12. The composition of claim 5 wherein the predetermined final pH is within a range of from about 2 to about 4.

13. The composition of claim 1 wherein the carrier provides for a dosage form selected from the group consisting of a lozenge, a chewing gum, and a quick-dissolving tablet.

14. The composition of claim 13 wherein the carrier provides for a lozenge.

15. The composition of claim 13 wherein the carrier provides for a quick-dissolving tablet.

16. The composition of claim 13 wherein the carrier provides for a chewing gum.

17. The composition of claim 16 wherein the carrier is a gum base.

18. The composition of claim 17 wherein the gum base comprises at least one hydrophobic polymer and at least one hydrophilic polymer.

19. The composition of claim 18, wherein the at least one hydrophilic polymer and the at least one hydrophobic polymer are independently selected from the group consisting of a natural polymer, a synthetic polymer, and mixtures thereof.

20. The composition of claim 19, wherein the at least one hydrophobic polymer is selected from the group consisting of a butadiene-styrene copolymer, butyl rubber, polyethylene, polyisobutylene, polyvinyl acetate phthalate, and mixtures thereof.

21. The composition of claim 20 wherein the hydrophobic polymer comprises a mixture of butyl rubber and polyisobutylene.

22. The composition of claim 1 wherein the buffer system favors at least 80% conversion of the ionized form to the un-ionized form.

23. The composition of claim 22 wherein the 80% conversion occurs in 10 minutes or less.

24. The composition of claim 1 wherein the buffer system favors at least 95% conversion of the ionized form to the un-ionized form.

25. The composition of claim 24 wherein the 95% conversion occurs in 10 minutes or less.

26. The composition of claim 1 wherein the buffer system favors at least 99% conversion of the ionized form into the un-ionized form.

27. The composition of claim 26 wherein the 99% conversion occurs in 10 minutes or less.

28. The composition of claim 1 wherein the buffering agents are selected from the group consisting of a mixture of a weak acid and a salt of weak acid, and a mixture of a base and a salt of a weak base.

29. The composition of claim 28 wherein the buffering agents are independently selected from the group consisting of sodium carbonate, sodium bicarbonate, potassium carbonate, potassium bicarbonate, potassium citrate and mono basic potassium phosphate, magnesium oxide, magnesium carbonate, magnesium bicarbonate, alkaline starch, ascorbic acid, and mixtures thereof.

30. The composition of claim 29 where one buffering agent is sodium bicarbonate and one buffering agent is sodium carbonate.

31. The composition of claim 29 where one buffering agent is potassium bicarbonate and one buffering agent is potassium carbonate.

32. The composition of claim 29 wherein the buffering agents are in weight ratio of from about 2-1:1-2.

33. The composition of claim 29 wherein the buffering agents are in weight ratio of from about 3-1:1-3.

34. The composition of claim 29 wherein the buffering agents are in weight ratio of from about 5-1:1-5.

35. The composition of claim 29 wherein the buffering agents are in weight ratio of from about 10-1:1-10.

36. The composition of claim 29 wherein the buffering agents are in a 1:1 ratio by weight.

37. The composition of claim 1 wherein the period of time for sustaining the predetermined final pH is at least 5 minutes.

38. The composition of claim 1 wherein the period of time for sustaining the predetermined final pH is at least 10 minutes.

39. The composition of claim 1 wherein the period of time for sustaining the predetermined final pH is at least 20 minutes.

40. The composition of claim 1 further comprising a penetration enhancer.

41. A chewing gum composition comprising:

at least one therapeutic agent at least partly in an ionized form, the ionized form capable of being converted into an un-ionized form;

a gum base;

a protecting agent, wherein the protecting agent coats at least a portion of the therapeutic agent and reduces adhesion between the therapeutic agent and the gum base; and

a buffer system,

wherein the buffer system comprises at least two different buffering agents and is capable of changing the pH of saliva from an arbitrary initial pH to a predetermined final pH, independent of the arbitrary initial pH, and of sustaining the predetermined final pH for a period of time, and

wherein the buffer system favors substantially complete conversion of the ionized form to the un-ionized form.

42. The chewing gum composition of claim 41 wherein the protecting agent comprises magnesium stearate.

43. The chewing gum composition of claim 41 wherein the gum base is mixed into the therapeutic agent during its formulation so that the therapeutic agent is in an excess amount relative to the gum base.

44. The composition of claim 41 wherein the gum base comprises at least one hydrophobic polymer and at least one hydrophilic polymer.

45. The composition of claim 44, wherein the at least one hydrophilic polymer and the at least one hydrophobic polymer are independently selected from the group consisting of a natural polymer, a synthetic polymer, and mixtures thereof.

46. The composition of claim 45, wherein the at least one hydrophobic polymer is selected from the group consisting of a butadiene-styrene copolymer, butyl rubber, polyethylene, polyisobutylene, polyvinyl acetate phthalate, and mixtures thereof.

47. The composition of claim 46 wherein the hydrophobic polymer comprises a mixture of butyl rubber and polyisobutylene.

48. The chewing gum composition of claim 41 further comprising a sweetener.

49. The chewing gum composition of claim 48 wherein the sweetener is selected from the group consisting of a mono-polysaccharide, di-polysaccharide, tri-polysaccharide, non-saccharide-based sweetener, dipeptide, chlorinated sugar derivative, sugar alcohol, hydrogenated starch hydrolysate, 3,6-dihydro-6-

methyl-1-1,2,3-oxathiazin-4-one-2,2-dioxide, and pharmaceutically acceptable salts, esters, analogs, and mixtures thereof.

50. The chewing gum composition of claim 41 further comprising a compound selected from the group consisting of a binder, a filler, a flavoring agent, a scenting agent, a coloring agent, a preservative, a plasticizer, a penetration enhancer, an elastomeric solvent, and mixtures thereof.

51. The chewing gum composition of claim 41 wherein the buffering agents are selected from the group consisting of a mixture of a weak acid and a salt of weak acid, and a mixture of a base and a salt of a weak base.

52. The chewing gum composition of claim 51 wherein the buffering agents are independently selected from the group consisting of sodium carbonate, sodium bicarbonate, potassium carbonate, potassium bicarbonate, potassium citrate and mono basic potassium phosphate, magnesium oxide, magnesium carbonate, magnesium bicarbonate, alkaline starch, ascorbic acid, and mixtures thereof.

53. The composition of claim 52 where one buffering agent is sodium bicarbonate and one buffering agent is sodium carbonate.

54. The composition of claim 52 where one buffering agent is potassium bicarbonate and one buffering agent is potassium carbonate.

55. The composition of claim 52 wherein the buffering agents are in weight ratio of from about 2-1:1-2.

56. The composition of claim 52 wherein the buffering agents are in weight ratio of from about 3-1:1-3.

57. The composition of claim 52 wherein the buffering agents are in weight ratio of from about 5-1:1-5.

58. The composition of claim 52 wherein the buffering agents are in weight ratio of from about 10-1:1-10.

59. The composition of claim 52 wherein the buffering agents are in a 1 to 1 ratio by weight.

60. The composition of claim 41 wherein the period of time for sustaining the predetermined final pH is at least 5 minutes.

61. The composition of claim 41 wherein the period of time for sustaining the predetermined final pH is at least 10 minutes.

62. The composition of claim 41 wherein the period of time for sustaining the predetermined final pH is at least 20 minutes.

63. The chewing gum composition of claim 41 wherein the at least one therapeutic agent is basic.

64. The chewing gum composition of claim 63 wherein the at least one therapeutic agent is selected from the group consisting of alfentanil, allylprodine, alphaprodine, anileridine, benzylmorphine, bezitramide, clonitazene, codeine, dextromoramide, diampromide, dihydrocodeine, dimenoxadol, dimepheptanol, dimethylthiambutene, dioxaphetyl butyrate, dipipanone, ethoheptazine, ethylmethylthiambutene, ethylmorphine, etonitazene, fentanyl, heroin, hydrocodone, isomethadone, levophenacylmorphan, lofentanil, meperidine, methadone, morphine, narceine, nicomorphine, norlevorphanol, normethadone, norpipanone, opium, oxycodone, papaveretum, phenadoxone, phenoperidine, piminodine, piritramide, propheptazine, promedol, properidine, propiram, propoxyphene, sufentanil, tramadol, tilidine, analogs, and mixtures thereof.

65. The chewing gum composition of claim 64 wherein the at least one therapeutic agent is oxycodone.

66. The chewing gum composition of claim 41 wherein the at least one therapeutic agent is acidic.

67. The composition of claim 66 wherein the at least one therapeutic agent is montelukast.

68. The composition of claim 41 wherein the at least one therapeutic agent is amphoteric.

69. The composition of claim 68 wherein the at least one therapeutic agent is selected from the group consisting of buprenorphine, butorphanol, cyclazocine, desomorphine, dezocine, dihydromorphine, eptazocine, hydromorphone, hydroxypethidine, ketobemidone, levallorphan, levorphanol, meptazinol, metazocine, metopon, morphine, nalbuphine, nalorphine, naloxone, naltrexone, normorphine, oxymorphone, pentazocine, phenomorphan, phenazocine, analogs, and mixtures thereof.